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WILSON SONSINI GOODRICH & ROSATI
650 PAGE MILL ROAD
PALO ALTO, CA 94304-1050

EXAMINER	
KIM, TAEYOON	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/530,164	BINDER ET AL.	
	Examiner	Art Unit	
	TAEYOON KIM	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 January 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *42,43,45-49 and 53-61* is/are pending in the application.

4a) Of the above claim(s) *60* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *42,43,45-49,53-59 and 61* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 42, 43, 45-49, and 53-61 are pending.

After further examination of the current application, the examiner decided to reopen the case, and therefore, the finality of that action is withdrawn.

However, the current claims are rejected based on new prior art found in during the further examination.

Applicant's amendment and response filed on 11/28/2007 has been received and entered into the case.

Claims 1-41, 50-52 have been canceled, claim 60 has been withdrawn from consideration as being drawn to non-elected subject matter, and claims 42, 43, 45-49, 53-59 and 61 have been considered on the merits. All arguments have been fully considered.

In the response to the claim rejection under 35 U.S.C. §112, 1st paragraph, new matter rejection, applicant argued that there are numerous disclosure in the specification. However, the specification does not contain such paragraphs as asserted by applicant.

In the response to the claim rejection under 35 U.S.C.§103 based on Liu in view of Dutt et al., applicant argued that there is no motivation to utilize amniotic membrane over collagen because the amniotic membrane has "inhibitory effect" on the growth of RPE cells. It is acknowledged that the reference (Dutt et al.) discloses less effective growth of RPE cells on the amniotic membrane compared to the collagen substrate. However, since the amniotic membrane can be used as a substrate to grow RPE cells,

although less effective than collagen, it would have been obvious to a person of ordinary skill in the art to replace the collagen substrate of Liu with the amniotic membrane of Dutt et al. for growth of RPE cells and subsequent transplantation into the eye. It is noted that although Dutt et al. teach away for the use of the amniotic membrane because of its inferior efficiency to collagen substrate, the amniotic membrane can be used for the same use as collagen,

M.P.E.P. §2145 states "A prior art reference that "teaches away" from the claimed invention is a significant factor to be considered in determining obviousness; however, "the nature of the teaching is highly relevant and must be weighed in substance. A known or obvious composition does not become patentable simply because it has been described as somewhat inferior to some other product for the same use." In re Gurley, 27 F.3d 551, 554, 31 USPQ2d 1130, 1132 (Fed. Cir. 1994) (Claims were directed to an epoxy resin based printed circuit material. A prior art reference disclosed a polyester-imide resin based printed circuit material, and taught that although epoxy resin based materials have acceptable stability and some degree of flexibility, they are inferior to polyester-imide resin based materials. The court held the claims would have been obvious over the prior art because the reference taught epoxy resin based material was useful for applicant's purpose, applicant did not distinguish the claimed epoxy from the prior art epoxy, and applicant asserted no discovery beyond what was known to the art.)."

Furthermore, the skilled artisan would have been motivated to replace collagen of Liu et al. with the amniotic membrane of Dutt et al. because it is well known in the art

that amniotic membrane is used for treating eye diseases as supported by Dua et al. and Young et al. (see below).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 42, 45, 47-49, 54, 59 and 61 are rejected under 35 U.S.C. 102(e) as being anticipated by Young et al. (WO 03/018040 A1) in light of Dua et al. (Br. J. Ophthalmol. 1999) or Tseng (US 6,152,142; IDS ref. #1).

Claims 42, 45, 47-49, 54, 59 and 61 are drawn to a method for treating a retinal disease, comprising inserting a composite comprising amniotic membrane and confluent retinal pigment epithelial cells in a subretinal space of a patient in need thereof; a limitation to the retinal disease being age-related macular degeneration; a limitation to the retinal pigment epithelial cells being cultured on the amniotic membrane; a limitation to the composite further comprising a pharmaceutically active molecule; a limitation to the pharmaceutically active molecule being growth factors, enzymes, or therapeutic drugs; a limitation to the amniotic membrane comprising a basement membrane and a stroma; a limitation to the retinal pigment epithelial equivalent cells being iris pigment epithelial cells, retinal pigment epithelial cells

differentiated from an adult or embryonic stem cell, cells derived from neural retinal cells or cell derived from a ciliary body; a limitation to the composite being formed by applying retinal pigment epithelial cell or its equivalent to an amniotic membrane, and culturing the cells on the membrane under the condition for growth.

Young et al. teach a method and a composite graft for the treatment of conditions associated with photoreceptor loss (e.g. age-related macular degeneration), where the composite graft comprising RPE cells grown on base membrane such as amniotic membrane (see abstract and p.12 lines 2-14). Young et al. also teach other types of cells including precursor to RPE cells or retina stem cells (see p.5, lines 10-14 and 18-19). Young et al. teach that the graft can be delivered to the subretinal space (see p.17, lines 7-8).

With regard to the term “confluent”, since it does not define the amount of confluence (e.g. 50% or 100%, etc.), the term is considered as any percentage of confluence for RPE cells.

With regard to the limitation of the presence of “pharmaceutically active molecule” in the composite of the method, it is considered that the limitation of “pharmaceutically active molecule” is an inherent property of the amniotic membrane of Young et al. as supported by Dua et al. Dua et al. teach that the amniotic membrane produces various growth factors such fibroblast growth factor (see p.748, right column, a section under the title of “Amniotic membrane in ophthalmology”). Fibroblast growth factor is considered to be a therapeutic drug. Furthermore, Young et al. teach the substrate (e.g. amniotic membrane) can also serve as a particularly convenient delivery

system for angiogenic/anti-angiogenic agents (therapeutic drugs) or other bioactive agents including (see p.12, lines 18- p.13, line 3).

Although Young et al. do not particularly teach the intact amniotic membrane having a basement membrane and a stroma, Tseng teaches that an amniotic membrane comprises two major components: the basement membrane and stroma (see col. 1, lines 23-24). Therefore, the amniotic membrane of Young et al. inherently comprises basement membrane and stroma.

Thus, the reference anticipates the claimed subject matter.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 42, 43, 45-49, 57-59 and 61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Young et al. (supra).

Claims 42, 43, 45-49, 57-59 and 61 are drawn to a method for treating a retinal disease, comprising inserting a composite comprising amniotic membrane and retinal pigment epithelial cells in a subretinal space of a patient in need thereof; a limitation to the epithelial cells being from about 16,000 to about 20,000 per 4 mm^2 of the amniotic membrane; a limitation to the retinal disease being age-related macular degeneration; a limitation to the amniotic membrane being human; a limitation to the retinal pigment epithelial cells being cultured on the amniotic membrane; a limitation to the amniotic

membrane being treated on one side with excimer laser ablation; a limitation to the excimer laser ablation altering the thickness of the stromal side or basement membrane of the amniotic membrane; a limitation to the retinal pigment epithelial equivalent cells being iris pigment epithelial cells, retinal pigment epithelial cells differentiated from an adult or embryonic stem cell, cells derived from neural retinal cells or cell derived from a ciliary body; a limitation to the composite being formed by applying retinal pigment epithelial cell or its equivalent to an amniotic membrane, and culturing the cells on the membrane under the condition for growth (claim 61).

Young et al. teach a method and a composite graft for the treatment of conditions associated with photoreceptor loss (e.g. age-related macular degeneration), where the composite graft comprising RPE cells grown on base membrane such as amniotic membrane (see abstract and p.12 lines 2-14). Young et al. also teach other types of cells including precursor to RPE cells (see p.5, lines 18-19). Young et al. teach that the graft can be delivered to the subretinal space (see p.17, lines 7-8). Young et al. also teach the membrane substrate can also serve as a particularly convenient delivery system for various bioactive agents (pharmaceutically active agents) such as growth factors (see p.12, line 18 through p.13, line 3).

Although Young et al. is silent in the concentration of RPE cells being confluent or 16,000 to about 20,000 per 4 mm^2 of amniotic membrane, the concentration of RPE cells required for the graft taught by Young et al. would be considered as a result-effective variable. As such, the variables would be routinely optimized by one of ordinary skill in the art in practicing the invention disclosed by those references.

Generally, differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 CCPA 1955) (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be prima facie obvious over a reference process which differed from the claims only in that the reference process was performed at a temperature of 100°C and an acid concentration of 10%.); >see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages."); ** In re Hoeschele, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969) (Claimed elastomeric polyurethanes which fell within the broad scope of the :references were held to be unpatentable thereover because, among other reasons, there was no evidence of the criticality of the claimed ranges of molecular weight or molar proportions.). For more recent cases applying this principle, see Merck & Co. Inc. v. Biocraft Laboratories Inc., 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989); In re Kulling, 897 F.2d 1147, 14 USPQ2d 1056 (Fed. Cir. 1990); and In re Geisler, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997). Accordingly, the claimed invention was prima facie obvious to one of ordinary skill in the art at the time the invention was made especially in the absence of evidence to the contrary.

With regard to the limitation of "human amniotic membrane" in claim 46, Young et al. do not particularly teach the source of the amniotic membrane. However, since Young et al. disclose the base membrane can be autologous to a patient, and it would have been obvious to a person of ordinary skill in the art to use human amniotic membrane for human patients.

With regard to the limitation in claims 57 and 58 drawn to the use of excimer laser, Young et al. do not particularly teach the limitation. However, it would have been obvious to a person of ordinary skill in the art to try excimer laser to trim and/or modify the base membrane suitable for transplantation because the excimer laser ablation technique is well known in the art to cut and reshape variety of tissues and laser treatment is commonly used for eye diseases as numerously disclosed in Young et al. (e.g. p.2, line 18). Since the technique is readily available in the art, and a person of ordinary skill in the art would recognize the technique suitable for modifying amniotic membrane, a person of ordinary skill in the art would choose to use the excimer laser technique in place of the surgical instrument for cutting the substrate for transplantation.

The Supreme Court recently states in KSR v. Teleflex (550 US82 USPQ2d 1385, 2007) "The same constricted analysis led the Court of Appeals to conclude, in error, that a patent claim cannot be proved obvious merely by showing that the combination of elements was "obvious to try." Id., at 289 (internal quotation marks omitted). When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success,

it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under §103."

The limitation of claim 58 is considered as a result of the method step in claim 57. Claim 58 contains a "wherein" clause that merely states the result of the limitations in the claim and therefore, adds nothing to the patentability or substance of the claim. Therefore, this phrase does not limit the claim. See *Texas Instruments Inc. v. International Trade Commission*, 26 USPQ2d 1010 (Fed. Cir. 1993); *Griffin v. Bertina*, 62 USPQ2d 1431 (Fed. Cir. 2002); *Amazon.com Inc. v. Barnesandnoble.com Inc.,* 57 USPQ2d 1747 (Fed. Cir. 2001).

Therefore, the invention as a whole would have been prima facie obvious to a person of ordinary skill at the time the invention was made.

Claim 53 is rejected under 35 U.S.C. 103(a) as being unpatentable over Young et al. (supra) in view of Grueterich et al. (2002; IDS ref. #28).

Claim 53 is drawn to a limitation to the amniotic membrane being epithelially denuded.

Young et al. render the subject matter of claim 42 obvious (see above).

Young et al. do not teach the amniotic membrane being epithelially denuded.

Grueterich et al. teach the use of epithelially denuded amniotic membrane in culturing limbal epithelium (see whole document; p.64, Materials and Method).

It would therefore have been obvious for the person of ordinary skill in the art at the time the invention was made to use epithelially denuded amniotic membrane of

Grueterich et al. in the method of Young et al.

The skilled artisan would have been motivated to make such a modification because both intact and epithelially denuded amniotic membrane would be suitable for support of epithelial cell culture. Since amniotic membrane is a suitable substrate for culturing not only corneal epithelial cells as taught by Grueterich et al. but also for RPE cells, a person of ordinary skill in the art would have considered the choice of intact or denuded amniotic membrane as a routine optimization procedure to obtain optimal environment for culturing RPE cells for treating a retinal disorder.

Therefore, the invention as a whole would have been prima facie obvious to a person of ordinary skill at the time the invention was made.

Claims 54-58 are rejected under 35 U.S.C. 103(a) as being unpatentable over Young et al. (supra) in view of Tseng (supra).

Claims 54-58 are drawn to a limitation the amniotic membrane being intact amniotic membrane comprising a basement membrane and a stroma; to the method further comprising a step of adding mesenchymal cells to one side of the stroma; a limitation to the mesenchymal cells being fibroblasts; a limitation to the amniotic membrane being treated with excimer laser ablation altering the thickness of the stromal side or basement membrane side of the amniotic membrane.

Young et al. teach the limitations of claim 42 (see above).

Although Young et al. do not particularly teach the intact amniotic membrane having a basement membrane and a stroma, Tseng teaches that an amniotic

membrane comprises two major components: the basement membrane and stroma (see col. 1, lines 23-24). Therefore, it would have been obvious to a person of ordinary skill in the art that the amniotic membrane of Young et al. inherently comprises basement membrane and stroma.

Young et al. do not teach a step of adding mesenchymal cells to the stroma of the amniotic membrane or the mesenchymal cells being fibroblasts.

Tseng teaches that when fibroblasts (mesenchymal cells) are grown in the stromal side of amniotic membrane, it provides an environment comparable to isolated collagen (fibroblasts are collagen-producing cells) and better cell growth in culture than a plain plastic surface.

It would therefore have been obvious for the person of ordinary skill in the art at the time the invention was made to add fibroblasts on the stromal side of the amniotic membrane of Young et al.

The skilled artisan would have been motivated to make such a modification because Tseng teaches an advantage given by the fibroblast culture on the stromal side of the amniotic membrane providing better cell culture environment for epithelial cells (see col. 4).

With regard to the limitation in claims 57 and 58 drawn to the use of excimer laser, Young et al. do not particularly teach the limitation. However, it would have been obvious to a person of ordinary skill in the art to try excimer laser to trim and/or modify the base membrane suitable for transplantation because the excimer laser ablation technique is well known in the art as supported by Tseng (e.g. col. 3, line 19) to cut and

reshape variety of tissues and laser treatment is commonly used for eye diseases as numerously disclosed in Young et al. (e.g. p.2, line 18). Since the technique is readily available in the art, and a person of ordinary skill in the art would recognize the technique suitable for modifying amniotic membrane, a person of ordinary skill in the art would choose to use the excimer laser technique in place of the surgical instrument for cutting the substrate for transplantation.

The Supreme Court recently states in KSR v. Teleflex (550 US82 USPQ2d 1385, 2007) "The same constricted analysis led the Court of Appeals to conclude, in error, that a patent claim cannot be proved obvious merely by showing that the combination of elements was "obvious to try." Id., at 289 (internal quotation marks omitted). When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under §103."

Therefore, the invention as a whole would have been prima facie obvious to a person of ordinary skill at the time the invention was made.

Claims 42, 43, 45-46, 49, 54, 57-59 and 61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Liu (US 6,045,791; IDS reference #7) in view of Dutt et al. (1991; IDS ref. #15) in further view of Dua et al. (supra) and Young et al. (supra).

Claims 42, 43, 45-46, 49, 54, 57-59 and 61 are drawn to a method for treating a retinal disease, comprising inserting a composite comprising amniotic membrane and retinal pigment epithelial cells in a subretinal space of a patient in need thereof (claim 42); a limitation to the epithelial cells being from about 16,000 to about 20,000 per 4 mm^2 of the amniotic membrane (claim 43); a limitation to the retinal disease being age-related macular degeneration (claim 45); a limitation to the amniotic membrane being human (claim 46); a limitation to the retinal pigment epithelial cells being cultured on the amniotic membrane (claim 47); a limitation to the composite further comprising a pharmaceutically active molecule (claim 48); a limitation to the pharmaceutically active molecule being growth factors, enzymes, or therapeutic drugs (claim 49); a limitation to the amniotic membrane comprising a basement membrane and a stroma (claim 54); a limitation to the amniotic membrane being treated on one side with excimer laser ablation (claim 57); a limitation to the excimer laser ablation altering the thickness of the stromal side or basement membrane of the amniotic membrane (claim 58); a limitation to the retinal pigment epithelial equivalent cells being iris pigment epithelial cells, retinal pigment epithelial cells differentiated from an adult or embryonic stem cell, cells derived from neural retinal cells or cell derived from a ciliary body (claim 59); a limitation to the composite being formed by applying retinal pigment epithelial cell or its equivalent to an amniotic membrane, and culturing the cells on the membrane under the condition for growth (claim 61).

Liu teaches a method of treating a retinal disorder such as age-related macular degeneration, by transplanting retinal pigment epithelium (RPE) cells cultured on an

attachment substrate into the subretinal area of a patient in need thereof (see Abstract and column 7, lines 57-59 and 65-67; Example 1).

Liu does not teach the use of amniotic membrane.

Dutt et al. teach the use of human amniotic membrane as a substrate for culturing retinal pigment epithelial cells (see whole document).

It would therefore have been obvious for the person of ordinary skill in the art at the time the invention was made to replace the collagen substrate of Liu with the amniotic membrane of Dutt et al. in the method of Liu.

The skilled artisan would have been motivated to make such a modification because both the substrate of Liu and the amniotic membrane of Dutt et al. are used for the growing RPE cells, they are considered as art-recognized equivalents for growing RPE cells for transplantation.

M.P.E.P. §2144.06 states "In re Scott, 323 F.2d 1016, 139 USPQ 297 (CCPA 1963) (Claims were drawn to a hollow fiberglass shaft for archery and a process for the production thereof where the shaft differed from the prior art in the use of a paper tube as the core of the shaft as compared with the light wood or hardened foamed resin core of the prior art. The Board found the claimed invention would have been obvious, reasoning that the prior art foam core is the functional and mechanical equivalent of the claimed paper core. The court reversed, holding that components which are functionally or mechanically equivalent are not necessarily obvious in view of one another, and in this case, the use of a light wood or hardened foam resin core does not fairly suggest the use of a paper core.); Smith v. Hayashi, 209 USPQ 754 (Bd. of Pat. Inter. 1980)

(The mere fact that phthalocyanine and selenium function as equivalent photoconductors in the claimed environment was not sufficient to establish that one would have been obvious over the other. However, there was evidence that both phthalocyanine and selenium were known photoconductors in the art of electrophotography. "This, in our view, presents strong evidence of obviousness in substituting one for the other in an electrophotographic environment as a photoconductor." 209 USPQ at 759.)."

With regard to the argument based on inferior property of the amniotic membrane compared to the collagen substrate taught by Dutt et al., teaching away to use the amniotic membrane over the collagen, although the amniotic membrane is less effective in proliferating RPE cells over the collagen substrate, it is recognized by a person of ordinary skill in the art that the amniotic membrane can be used for the same purpose as the collagen substrate. M.P.E.P. §2145 states "A prior art reference that "teaches away" from the claimed invention is a significant factor to be considered in determining obviousness; however, "the nature of the teaching is highly relevant and must be weighed in substance. A known or obvious composition does not become patentable simply because it has been described as somewhat inferior to some other product for the same use." In re Gurley, 27 F.3d 551, 554, 31 USPQ2d 1130, 1132 (Fed. Cir. 1994) (Claims were directed to an epoxy resin based printed circuit material. A prior art reference disclosed a polyester-imide resin based printed circuit material, and taught that although epoxy resin based materials have acceptable stability and some degree of flexibility, they are inferior to polyester-imide resin based materials. The court held the

claims would have been obvious over the prior art because the reference taught epoxy resin based material was useful for applicant's purpose, applicant did not distinguish the claimed epoxy from the prior art epoxy, and applicant asserted no discovery beyond what was known to the art.).

Furthermore, the skilled artisan would have been motivated to replace collagen of Liu with the amniotic membrane of Dutt et al., because it is well known in the art that amniotic membrane is used for treating eye diseases as supported by Dua et al. Dua et al. teach the amniotic membrane serves as a transplanted basement membrane which facilitates migration of epithelial cells, and further the presence of various growth factors in the amniotic membrane can stimulate epithelization (see p.748 under "Amniotic membrane in ophthalmology"). Still further Young et al. teach that the amniotic membrane is an equivalent for the Bruch's membrane (see abstract and p.12 lines 2-14). Thus, a person of ordinary skill in the art would recognize the amniotic membrane as an equivalent to the Bruch's membrane, which is a natural substrate for RPE cells in vivo, and

Although Liu in view of Dutt et al. in further view of Dua et al. and Young et al. do not particularly teach the number of cells on the amniotic membrane, however, because the number of cells used in the claimed method is considered as one of result effective variables. As such, the variables would be routinely optimized by one of ordinary skill in the art in practicing the invention disclosed by those references. Generally, differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical. "[W]here the

general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 CCPA 1955) (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be prima facie obvious over a reference process which differed from the claims only in that the reference process was performed at a temperature of 100°C and an acid concentration of 10%.); >see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages."); ** In re Hoeschele, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969) (Claimed elastomeric polyurethanes which fell within the broad scope of the :references were held to be unpatentable thereover because, among other reasons, there was no evidence of the criticality of the claimed ranges of molecular weight or molar proportions.). For more recent cases applying this principle, see Merck & Co. Inc. v. Biocraft Laboratories Inc., 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989); In re Kulling, 897 F.2d 1147, 14 USPQ2d 1056 (Fed. Cir. 1990); and In re Geisler, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997). Accordingly, the claimed invention was prima facie obvious to one of ordinary skill in the art at the time the invention was made especially in the absence of evidence to the contrary.

With regard to the limitation of the presence of “pharmaceutically active molecule” in the composite of the method, it is considered that the limitation of

"pharmaceutically active molecule" is inherently accomplished by the use of amniotic membrane of Dutt et al. in the method of Liu. Because Dua et al. teach the amniotic membrane produces various growth factors such fibroblast growth factor (see p.748, right column, a section under the title of "Amniotic membrane in ophthalmology").

Although Liu in view of Dutt et al. in further view of Dua et al. and Young et al. do not particularly teach the use of excimer laser ablation technique, since it is necessary to cut the substrate, having RPE cells grown on it, for transplantation as described in Liu (see Example 1, column 11, lines 10-11), and excimer laser ablation technique is well known in the art to cut and reshape variety of tissues, it would have been obvious for a person of ordinary skill in the art to optimize the cutting procedure by using a technique with high precision such as excimer laser ablation technique. Further, a surgical instrument used in the method of Liu for cutting the substrate containing RPE cells and excimer laser ablation would be considered as art-recognized equivalents, and therefore, the excimer laser ablation would be used in place of the surgical instrument for cutting the substrate for transplantation.

The limitation of claim 58 is considered as a result of the method step in claim 57. Claim 58 contains a "wherein" clause that merely states the result of the limitations in the claim and therefore, adds nothing to the patentability or substance of the claim. Therefore, this phrase does not limit the claim. See *Texas Instruments Inc. v. International Trade Commission*, 26 USPQ2d 1010 (Fed. Cir. 1993); *Griffin v. Bertina*, 62 USPQ2d 1431 (Fed. Cir. 2002); *Amazon.com Inc. v. Barnesandnoble.com Inc.,* 57 USPQ2d 1747 (Fed. Cir. 2001).

Therefore, the invention as a whole would have been prima facie obvious to a person of ordinary skill at the time the invention was made.

Claim 53 is rejected under 35 U.S.C. 103(a) as being unpatentable over Liu (supra) in view of Dutt et al. (supra), in further view of Dua et al. (supra), Young et al. (supra) and Grueterich et al. (2002; IDS ref. #28).

Claim 53 is drawn to a limitation to the amniotic membrane being epithelially denuded.

Liu in view of Dutt et al. in further view of Dua et al. and Young et al. render the subject matter of claim 42 obvious (see above).

Liu in view of Dutt et al. in further view of Dua et al. and Young et al. do not teach the amniotic membrane being epithelially denuded.

Grueterich et al. teach the use of epithelially denuded amniotic membrane in culturing limbal epithelium (see whole document; p.64, Materials and Method).

It would therefore have been obvious for the person of ordinary skill in the art at the time the invention was made to use epithelially denuded amniotic membrane of Grueterich et al. in the method of Liu in view of Dutt et al. in further view of Dua et al. and Young et al.

The skilled artisan would have been motivated to make such a modification because both intact and epithelially denuded amniotic membrane would be suitable for support of epithelial cell culture. Since amniotic membrane is a suitable substrate for culturing not only corneal epithelial cells as taught by Grueterich et al. but also for RPE

cells, a person of ordinary skill in the art would have considered the choice of intact or denuded amniotic membrane as a routine optimization procedure to obtain optimal environment for culturing RPE cells for treating a retinal disorder.

Therefore, the invention as a whole would have been prima facie obvious to a person of ordinary skill at the time the invention was made.

Claims 55 and 56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Liu (supra) in view of Dutt et al. (supra), in further view of Dua et al. (supra) Young et al. (supra) and Tseng (supra).

Claims 55 and 56 are drawn to a limitation to the method further comprising a step of adding mesenchymal cells to one side of the stroma (claim 55); a limitation to the mesenchymal cells being fibroblasts (claim 56);

Liu in view of Dutt et al. in further view of Dua et al. and Young et al. render the subject matter of claim 42 obvious (see above).

Liu in view of Dutt et al. in further view of Dua et al. and Young et al. do not teach a step of adding mesenchymal cells to the stroma of the amniotic membrane or the mesenchymal cells being fibroblasts.

Tseng teaches that when fibroblasts (mesenchymal cells) are grown in the stromal side of amniotic membrane, it provides an environment comparable to isolated collagen (fibroblasts are collagen-producing cells) and better cell growth in culture than a plain plastic surface.

It would therefore have been obvious for the person of ordinary skill in the art at

the time the invention was made to add fibroblasts on the stromal side of the amniotic membrane of Liu in view of Dutt et al. in further view of Dua et al. and Young et al.

The skilled artisan would have been motivated to make such a modification because Tseng teaches an advantage given by the fibroblast culture on the stromal side of the amniotic membrane providing better cell culture environment for epithelial cells.

Therefore, the invention as a whole would have been prima facie obvious to a person of ordinary skill at the time the invention was made.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TAEYOON KIM whose telephone number is (571)272-9041. The examiner can normally be reached on 8:00 am - 4:00 pm ET (Mon-Thu).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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/Leon B Lankford Jr/
Primary Examiner, Art Unit 1651

Taeyoon Kim
AU-1651